

Study of Predictors for Ventilatory Support in Patients of Organophosphorus Compound Poisoning.

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ABSTRACT

Background: Organophosphorus compound poisoning is used most commonly for suicidal attempts which is seen frequently in farmers of younger age group of lower socio-economic status from rural areas. The aim of study is to know the clinical profile of organophosphate compound poisoning and to identify the factors which help in predicting the need for ventilatory support in this poisoning. **Methods:** A hospital based prospective cross sectional study was conducted with 100 patients to analyze the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorus compound poisoning. **Results:** Majority of the patients were in the age group of 21-30 years. The mean age of the patients was 31.96 ± 14.12 years. The route of exposure was oral in all the patients. The most common organophosphorus compound consumed in our study was Malathion (28%) ,46 (46%) patients had very poor GCS score (≤ 7), 38 (38%) patients had low serum cholinesterase levels (≤ 2100 IU/L),9 (9%) patients had amylase levels > 140 U/L, 43 (43%) patients required ventilatory support while 57 (57%) patients did not require ventilator support. Among patients with fasciculations 64% were on ventilatory support. There was significant association of fasciculations and ventilatory support. 87 (87%) patients survived while 13 (13%) patients died in our study. All patients that died were on ventilatory support. **Conclusion:** Clinical and biochemical parameters such as greater the time lag from consumption of OP poison till getting specific treatment, Lower GCS scoring, Generalized Fasciculation's, Low cholinesterase levels were strong predictors for the need for Assisted Ventilation in OP poisoning.

Keywords: Organophosphorus, poisoning, ventilation.

INTRODUCTION

India being an agriculture-based country, organophosphate (OP) pesticide remains the main agent for crop protection and pest control. It is therefore likely to have adverse effects on farmers who are accidentally over exposed while handling these pesticides. However, because of low cost and easy availability, it has also become an agent of choice for self poisoning.^[1-3]

Organophosphates are one of the common causes of suicidality worldwide. Gunnell et al. have reported that there are 258,234 deaths each year from organophosphate poisoning, which accounts for about 30% of the suicidal cases globally.^[4] OPs result in phosphorylation of serine hydroxyl residue on acetylcholine esterase enzyme, which results in the accumulation of acetylcholine.

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This leads to cholinergic features, which can be classified into central and peripheral. Peripheral events include vomiting, diarrhea, miosis, muscle fasciculations, urinary incontinence, and bronchoconstriction. Central effects include respiratory depression and delirium.^[5]

One of the devastating cholinergic features of organophosphate poisoning is respiratory failure. There are several explanations for respiratory failure; central, as well as peripheral mechanisms, underlie this phenomenon. However, studies have suggested that the major mechanisms regulating respiratory failure associated with OP ingestion are central in origin. The respiratory center known as the pre-Botzinger complex is situated in the ventrolateral medulla. It is composed of glutaminergic and muscarinic fibers. Excess acetylcholine can depress respiratory activity in these areas.^[6-7] Injection of dichlorvos bilaterally into the pre-Botzinger complex in vagally intact rats produces a decrease in respiratory rate, a decrease in volume of inspired gas, and about 27% of the animals became apneic.^[8-10]

Vagus is the major neural pathway that interconnects the brain and lung. Mechanoreceptors provide feedback via the vagus nerve. Vagal mechanisms blunt the hypoventilation associated with OPs in spontaneously breathing animals. Vagal mechanisms also cause an increase in pulmonary secretions due to pulmonary irritants, and surgical vagotomy has been shown to decrease pulmonary secretions.^[11]

OP exposure to the lung causes increased acetylcholine at the pulmonary muscarinic receptors causing pulmonary abnormalities. OP agents increase the work of breathing through an increase in pulmonary static and dynamic compliance and by causing obstruction of airways.^[12-14] OPs have the tendency to cause interstitial edema, which is responsible for the decrease in pulmonary compliance and ventilation-perfusion (V/Q) mismatch.^[15,16]

Hence the present study was done at our tertiary care centre to assess the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning.

MATERIALS AND METHODS

A hospital based prospective cross sectional study was conducted with 100 patients admitted in BLDE Hospital to analyze the clinical profile of organophosphate compound poisoning and identify the factors which help in predicting the need for ventilatory support in organophosphorous compound poisoning.

Statistical Analysis

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of Fisher test, student 't' test and Chi-Square test. 'p' value less than 0.05 is taken as significant.

Pearson's chi-squared test

$$X^2 = \sum_{i=1}^n \frac{(O_i - E_i)^2}{E_i}$$

Where X^2 = Pearson's cumulative test statistic.

O_i = an observed frequency;

E_i = an expected frequency, asserted by the null hypothesis;

n = the number of cells in the table.

Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 is used for statistical analysis. Graphical representation has been done in MS Excel 2010.

RESULTS

Distribution of patients according to Age

Majority of the patients (41%) were in the age group of 21-30 years followed by 11-20 years (23%), 31-40 years (18%), 51-60 years (9%), 41-50 years (6%) and >60 years (3%). The mean age of the patients was 31.96 ± 14.12 years.

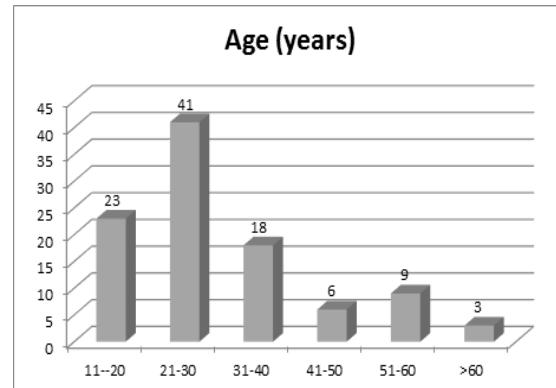


Figure 1: Distribution of patients according to Age

Distribution of patients according to Sex

In this study 38% patients were male and 62% were female. There was female preponderance in our study and the M:Fratio was 1:1.6. The route of exposure was oral in all the patients.

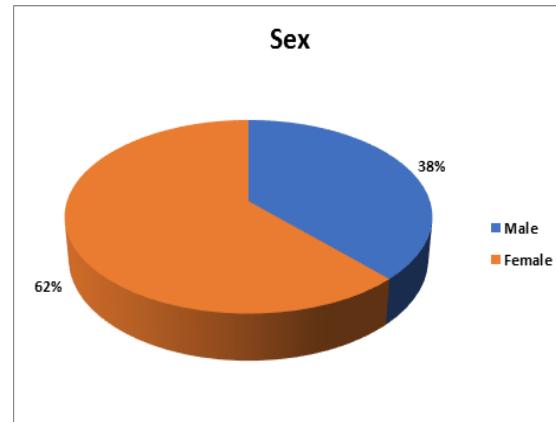


Figure 2: Distribution of patients according to Sex

Distribution of patients according to Type of Compound Consumed

The most common organophosphorus compound consumed in our study was Malathion (28%) followed by Dichlorovas (25%), Monocrotophos (24%), Dimethoate (6%) and Methyleparathion (5%).

Table 1: Distribution of patients according to Type of Compound Consumed.

Type of Compound	N	%
Chlorpyriphos	2	2
Dichlorovas	25	25
Dimethoate	6	6
Malathion	28	28
Methyleparathion	5	5

Monocrotophos	24	24
Paration	1	1
Phenylphyrazole	1	1
Phorate	1	1
Phosphonic Acid	1	1
Prophenofus+Cypermethrin	2	2
Quinphos	1	1
Triazophos	2	2
Unknown Compound	1	1
Total	100	100

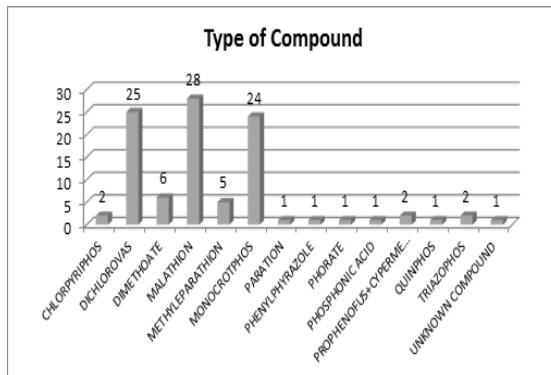


Figure 3: Distribution of patients according to Type of Compound Consumed

Distribution of patients according to effect of OP poisoning

The most common effect of OP poisoning was pinpoint pupils (74%) followed by respiratory failure (42%), fasciculations (11%) and intermediate syndrome (2%).

Table 2: Distribution of patients according to effect of OP poisoning

Effect of OP poisoning	N	%
Pinpoint pupils	74	74
Respiratory Failure	43	43
Fasciculations	11	11
Intermediate syndrome	2	2

Distribution of patients according to Glasgow Coma Scale (GCS)

46 (46%) patients had very poor GCS score (≤ 7) while 53 (53%) patients had GCS score between 8 to 11. 1 (1%) patient had good GCS score (12-15).

Table 3: Distribution of patients according to Glasgow Coma Scale (GCS)

Glasgow Coma Scale	N	%
≤ 7	46	46
8-11	53	53
12-15	1	1
TOTAL	100	100

Distribution of patients according to Serum Cholinesterase levels

38 (38%) patients had low serum cholinesterase levels (≤ 2100 IU/L) while 62 (62%) patients had serum cholinesterase levels > 2100 IU/L.

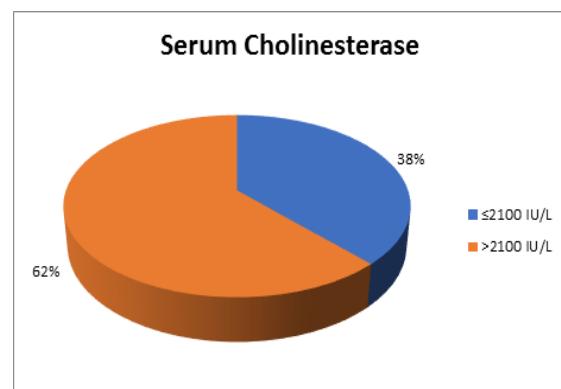


Figure 4: Distribution of patients according to Serum Cholinesterase levels

Distribution of patients according to Amylase levels

91 (91%) patients had amylase levels in the normal range (40-140 U/L) while 9 (9%) patients had amylase levels > 140 U

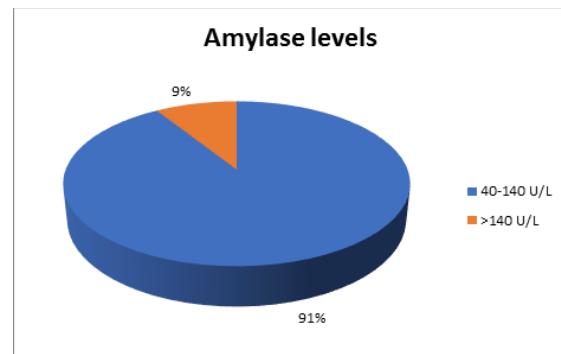


Figure 5: Distribution of patients according to Amylase levels

Distribution of patients according to Time Interval between Consumption and Hospital Admission

Majority of the patients (71%) were admitted in the hospital within 2-4 hours of ingesting organophosphorus poison while 18 (18%) and 9 (9%) patients were admitted within 4-8 hours and < 2 hours. 2 (2%) patients were admitted after > 8 hours of ingesting organophosphorus poison.

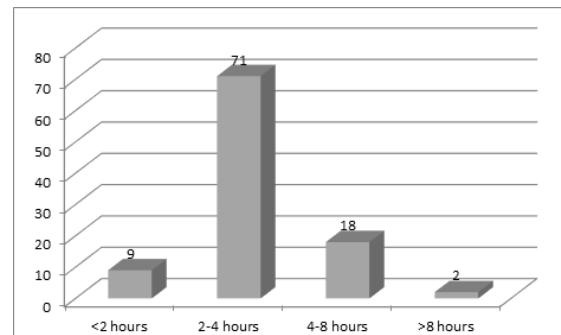


Figure 6: Distribution of patients according to Time Interval between Consumption and Hospital Admission

Distribution of patients according to Requirement of Ventilatory Support

43 (43%) patients required ventilatory support while 57 (57%) patients did not require ventilator support.

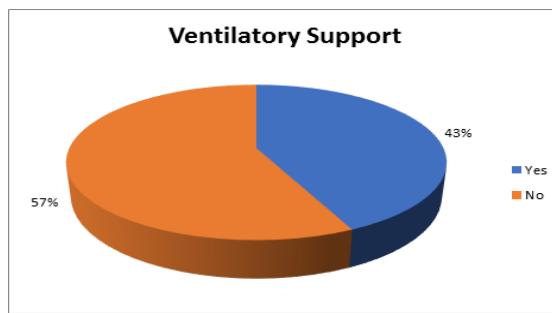


Figure 7: Distribution of patients according to Requirement of Ventilatory Support

Distribution of patients according to Outcome

87 (87%) patients survived while 13 (13%) patients died in our study.

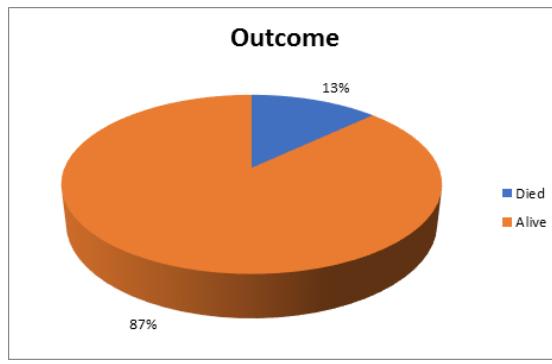


Figure 8: Distribution of patients according to Outcome

Association of Pinpoint pupils and Ventilatory Support

Among patients with pinpoint pupils 41(55.4%) were not on ventilatory support however there was no significant association of pinpoint pupils and ventilatory support as per Chi-square test ($p>0.05$).

Association of Respiratory Failure and Ventilatory Support

Among all patients 33 were on ventilatory support with respiratory failure, while 10 were not on ventilatory support with respiratory failure. There was significant association of respiratory failure and ventilatory support as per Chi-square test ($p<0.05$).

Association of Fasciculations and Ventilatory Support

Among all patients 11 were on ventilatory support with fasciculations, while there was no case without ventilatory support with fasciculations. There was significant association of fasciculations and ventilatory support as per Chi-square test ($p<0.05$).

Association of Glasgow Coma Scale (GCS) and Ventilatory Support

Majority of patients with very poor GCS score (67.4%) were on ventilatory support. There was significant association of Glasgow Coma Scale (GCS) and ventilatory support as per Chi-square test ($p<0.05$).

Association of Amylase levels and Ventilatory Support

Among patients with high amylase levels, 7 (16.3%) patients were on ventilatory support while 2 (3.5%) patients were not on ventilatory support. There was significant association of amylase levels and ventilatory support as per Chi-square test ($p<0.05$).

Association of Serum Cholinesterase levels and Ventilatory Support

Majority of the patients on ventilatory support had low serum cholinesterase levels (69.8%). There was significant association of serum cholinesterase levels and ventilatory support as per Chi-square test ($p<0.05$).

Association of Time Interval between Consumption and Hospital Admission and Ventilatory Support

There was significant association of time interval between consumption and hospital admission and ventilatory support as per Chi-square test ($p<0.05$).

Association of Outcome and Ventilatory Support

All patients that died were on ventilatory support. There was significant association of outcome and ventilatory support as per Chi-square test ($p<0.05$).

Multivariate analysis for predictors of Ventilatory Support

Logistic regression analysis was used to evaluate predictors of ventilatory support. The logistic regression analysis showed that respiratory failure, fasciculations, Glasgow Coma Scale, serum cholinesterase and time interval between consumption and hospital admission were independently associated with ventilatory support.

Table 4: Association of Pinpoint pupils and Ventilatory Support

Pinpoint pupils	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
NO	10	38.5	16	61.5	26	26.0	>0.05	
YES	33	44.6	41	55.4	74	74.0		
Total	43	43.0	57	57.0	100	100.0		

Table 5: Association of Respiratory Failure and Ventilatory Support

Respiratory Failure	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
NO	10	17.5	47	82.5	57	57.0	<0.05	
YES	33	76.7	10	23.3	43	43.0		
Total	43	43.0	57	57.0	100	100.0		

Table 6: Association of Fasciculations and Ventilatory Support

Fasciculations	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
NO	32	36.0	57	64.0	89	89.0	<0.05	
YES	11	100.0	0	0.0	11	11.0		
Total	43	43.0	57	57.0	100	100.0		

Table 7: Association of GCS and Ventilatory Support

GCS	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
≤7	29	67.4	17	29.8	46	46.0	<0.05	
8-11	14	32.6	39	68.4	53	53.0		
12-15	0	0.0	1	1.8	1	1.0		
Total	43	100.0	57	100.0	100	100.0		

Table 8: Association of Serum Cholinesterase levels and Ventilatory Support

Serum Cholinesterase levels	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
≤2100 IU/L	30	69.8	8	14.0	38	38.0	<0.05	
>2100 IU/L	13	30.2	49	86.0	62	62.0		
Total	43	100.0	57	100.0	100	100.0		

Table 9: Association of Amylase levels and Ventilatory Support

Amylase levels	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
40-140 U/L	36	83.7	55	96.5	91	91.0	<0.05	
>140 U/L	7	16.3	2	3.5	9	9.0		
Total	43	100.0	57	100.0	100	100.0		

Table 10: Association of Time Interval between Consumption and Hospital Admission and Ventilatory Support

Time Interval	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
<2 hours	2	22.2	7	77.8	9	9.0	<0.05	
2-4 hours	30	42.3	41	57.7	71	71.0		
4-8 hours	9	50.0	9	50.0	18	18.0		
>8 hours	2	100.0	0	0.0	2	2.0		
Total	43	43.0	57	57.0	100	100.0		

Table 11: Association of Outcome and Ventilatory Support

Outcome	Ventilatory Support						p Value	
	Yes		No		Total			
	N	%	N	%	N	%		
Died	13	30.2	0	0.0	13	13.0	<0.05	
Alive	30	69.8	57	100.0	87	87.0		
Total	43	100.0	57	100.0	100	100.0		

Table 12: Multivariate analysis for predictors of Ventilatory Support

Parameters	OR	95% CI	p Value
Age	0.75	0.54–1.03	p>0.05
Sex	1.23	1.00–1.51	p>0.05
Pinpoint pupils	1.17	0.45–2.85	p>0.05
Respiratory Failure	1.70	1.15–2.50	p<0.05
Fasciculations	1.50	1.28–1.75	p<0.05
Glasgow Coma Scale	1.12	1.01–1.25	p<0.05
Serum Cholinesterase	2.70	2.33–3.13	p<0.05
Amylase	0.81	0.61–1.09	p>0.05
Time Interval between Consumption and Hospital Admission	1.42	1.26–1.60	p<0.05

DISCUSSION

OP compounds were synthesized by von Hoffman. OP pesticide poisoning is common in developing worlds. The highest incidence is seen in India. Suicidal and non-suicidal organophosphate poisoning is a major problem in rural areas of India, with rapidly increasing incidence rate.^[17]

Chowdhary AN et al,^[2] prospective study reported incidence of suicidal poisoning is 98.6%, probably because it is cheap, easily available and used as a major pesticide in agricultural farming throughout India.

The leading cause of death in OP poisoning is respiratory failure¹⁸⁻²⁰ and various grading systems proposed suggest that most cases can be managed in the ICU.

Tsao TC et al,^[21] prospective study evaluating various parameters that can predict outcome of patients in OP poisoning found one hundred two (76.7%) were males and 31 (23.3%) female. Most of the cases were young people 80% (< 40 years) predominantly males. There was wide variation in age ranging from a minimum of 13-68 years with mean age of 31.5 years.

Fryer AD et al^[22] descriptive study assessing clinical and biochemical parameters in organophosphate poisoning, which help to predict the need for ventilator support observed maximum number of cases was 21-30 years in the age group of years, youngest patient in present study was 14 years and the oldest patient in this study was 68 years. Out of 50 cases 33 were Males (66%) and 17 were females (34%).

Rodger ML et al,^[18] descriptive study assessing clinical and biochemical parameters in organophosphate poisoning, which help to predict the need for ventilator support reported Methyl parathion was the commonest poisoning encountered; out of 25 cases 15 cases required ventilator support. Among 6 cases of Dimethoate poisoning, 4 cases (66.7) required ventilator support. Shetti AN et al,^[22] prospective, observational, descriptive, intention to-treat study reported around 68% of patient presented with bradycardia, 28% of patients with miosis, 28% of patients with altered sensorium, 21% of patient with tachypnea, 15% of patient fasciculation and 10% of patients with seizures.

Chethan RAN et al,^[23] prospective, observational, descriptive, intention to-treat study observed mean serum pseudocholinesterase level in mild poisoning was 5680.653U/L, moderate poisoning was 4707 U/L, severe poisoning was 175.133 U/L.

Rajeev H et al,^[24] prospective study evaluating various parameters that can predict outcome of patients in OP poisoning reported fifty three patients required ventilatory support, out of which only 11 patients survived. Patients were on ventilator support

for minimum 1 day to maximum 22 days with a mean 6.85 ± 4.32 days. Mortality was higher in patients who required ventilator support >7 days [$P < 0.05$ statistically significant].

Shetti AN et al,^[22] retrospective study correlating the serum acetylcholinesterase levels with morbidity, ventilation need, ICU stay and the final outcome of the ailment reported 10 (40%) male patients died and 2 (28.5%) female patients died.

Rajeev H et al,^[24] descriptive study assessing clinical and biochemical parameters in organophosphate poisoning, which help to predict the need for ventilator support reported mortality of 16% (4 out of 24 Ventilated patients)

Chethan RAN et al,^[23] prospective, observational, descriptive, intention to-treat study reported most of the patients (73%) recovered completely and discharged without ventilator support, their serum pseudocholinesterase level was above 5000 U/L, POPScore was below 5 and Mean duration of hospital was 5days. The longest hospital stay was of a male patient who had consumed parathion and was in hospital for 55 days (POP scale 9). He presented with respiratory failure within 6 hours of consumption and was intubated for 13 days and tracheostomy was done and had complete recovery and discharged after 55 days. 27% of patients required ventilator support. Death has occurred in 10% of patients. POP Score in death patients was above 8, mean pseudo-cholinesterase level was 571U/L.

Patil SL et al,^[25] descriptive study assessing clinical and biochemical parameters in organophosphate poisoning, which help to predict the need for ventilator support reported survival rate after ventilator support was better with methyl parathion poisoning, 25 out of 50(50%) while Fenithrothion (Tik -20) poisoning was second commonest; 12 out of 50 (24%) cases. The survival rate after ventilator support was better with methyl parathion poisoning 22 out of 25 patients survived while in Dimethoate poisoning where 4 out of 6 patients survived

CONCLUSION

OP insecticide poisoning is a life threatening condition that needs rapid diagnosis and treatment. Since most of the patients present with respiratory failure, early initiation of mechanical ventilation plays a vital role in the treatment of such cases. Emphasis must also be given to good supportive care and monitoring for the prevention and management of acute and delayed complications that occur during the course of stay in ICU.

Clinical and biochemical parameters such as greater the time lag from consumption of OP poison till getting specific treatment, Lower GCS scoring, Generalized Fasciculation's, Low Pseudo

cholinesterase levels were strong predictors for the need for Assisted Ventilation in OP poisoning. Grading of the severity of the OP compound poisoning taking the above parameters into consideration can help to identify high risk patients who may go in for Respiratory failure and require ICU admission and Ventilator support.

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